Circulating endothelial progenitor cells decrease in patients after endarterectomy

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Background: **Endothelial progenitor cells (EPC) contribute to vascular regeneration. Since surgical injury and burns induce a pro-inflammatory and proangiogenic response, we investigated the effect of vascular injury with minimal surgical trauma after endarterectomy on the number of circulating EPC and systemic inflammatory changes.**

Methods and Results: **Forty-five patients with peripheral arterial occlusive disease were included in the study. Venous blood samples were taken before and 1 day after endarterectomy and plaque material was obtained. Ten patients with minor surgery served as controls. Circulating CD133+CD34+, VEGFR-2+CD34+ progenitor cells and surface expression of CD11b on circulating neutrophils were analysed using flow cytometry. EPCs were characterized in a culture assay as double-positive for DiI-LDL uptake and lectin binding. Cytokine concentrations of interleukin (IL)-6, IL-8, TNF-α, IL-1ß, IL-10, IL-12, SDF-1, G-CSF, and VEGF were measured in plasma and tissue samples. After endarterectomy a significant decrease in circulating EPC, CD133+CD34+, and VEGFR-2+CD34+ cells was observed. This was associated with a specific pattern of changes in circulating cytokine levels after endarterectomy with a decrease in IL-1 beta and IL-12, an increase in IL-6 and G-CSF plasma concentrations, and surface expression of CD11b on circulating neutrophils. In contrast, after minor surgery an increase in circulating CD133+CD34+ cells, IL-6, IL-8, and IL-10 was found. Interestingly there was a negative association between levels of local IL-6 within the plaque and only the preoperative levels of circulating CD133+C34+.**

Conclusion: **Endarterectomy induces changes in circulating cytokines and a decline in circulating progenitor cells, which may be due to recruitment of progenitor cells to the injured vessels. This is supported by the negative association between plaque inflammation and circulating progenitor cells before endarterectomy. (J Vasc Surg 2008;48:1217-22.)**

Endothelial progenitor cells (EPCs) represent a potential repair mechanism of the organism for vascular lesions. Tissue damage such as myocardial infarction,[1] severe burns, or bypass surgery[2] increase the number of circulating endothelial progenitor cells. Mobilized from the bone marrow, progenitor cells are recruited to ischemic areas through specific chemokine and integrin interactions[3] and contribute to neovascularization and tissue regeneration.[4] Increased progenitor cell release from the bone marrow is part of the host defense during inflammation as a result of injury-mediated release of stress signals. This release is induced by a wide range of cytokines such as granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), stem cell factor (SCF), and chemokines such as interleukin (IL)-8, Mip-1α, Gro-ß, and stromal derived factor (SDF)-1.[3]

In this study, one aim was to investigate the influence of vascular injury induced by endarterectomy and its effect on circulating hematopoietic CD34+CD133+ and endothelial CD34+VEGFR2+ progenitor cells.

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Atherosclerosis was identified as a disease not only due to lipid accumulation, but as a process of endothelial dysfunction and subendothelial inflammation resulting in regenerative responses of the vessel wall. Local release of mediators from endothelial cells and leukocytes within atherosclerotic plaques is fundamental for plaque progression.[5,6] Epidemiological studies showed an increased vascular risk for patients with elevated acute-phase proteins such as C-reactive protein and different cytokines like IL-6 and TNF-α.[7] Previous investigations including patients undergoing endarterectomy mainly explored histological composition of atherosclerotic plaque material and local cytokine expressions.

In this study, in addition to the local inflammation of atherosclerotic plaques, the systemic inflammatory reaction and its cytokine pattern after endarterectomy were examined. Furthermore, we sought to investigate the association between circulating endothelial and hematopoietic progenitor cells and systemic or local inflammation.

METHODS

Patient selection. The study group comprised of 45 patients with symptomatic peripheral arterial occlusive disease with stenosis ranging from 85-99% undergoing endarterectomy of carotid, iliac, or femoral artery. Stenosis of 85% or more was confirmed either by catheter angiography, duplex scanning, or magnetic resonance angiography of the respective artery. To minimize confounding factors, patients with chronic inflammatory disease or acute ischemia were excluded. Carotid endarterectomy was performed in "no touch" technique, using a shunt to maintain sufficient

cerebral blood flow after carotid clamping and conventional open endarterectomy with longitudinal arteriotomy and closure by a collagen coated Dacron patch. Endarterectomy of femoral and iliac artery was performed using a semi-closed technique and a Vollmar ringstripper according to customary practice. Venous blood samples were taken on admission and 15-18 hours after endarterectomy. Excised atherosclerotic plaque material was attained during surgery. To estimate the impact of surgery without extensive vascular injury, a control group comprising of 10 patients with elective implantation of a pacemaker or an internal defibrillator device was analyzed. The study protocol was approved by the institutional ethics committee and informed consent was obtained from all subjects.

Immunoassays. Serum from venous blood samples were frozen and stored at −80°C. Concentrations of IL-1ß, TNF-α, IL-6, IL-8, IL-10, IL-12, and G-CSF were determined by immunoassays (CBA Human Inflammation Kit, BD Biosciences, San Diego, Calif; G-CSF Immunoassay Quantikine R&D Systems, Minneapolis, Minn). Detection limits were 2.5 pg/mL for IL-6, 3.6 pg/mL for IL-8, 3.3 pg/mL for IL-10, 1.9 pg/mL for IL-12, 7.2 pg/mL for IL-1ß, 3.7 pg/mL for TNF-α, and 20 pg/mL for G-CSF. Intra-assay variability for the lower assay range were <10%.

Atherosclerotic plaque material. The atherosclerotic plaque material was attained during surgery, then frozen and stored at -80°C. Afterwards, atherosclerotic tissue was lysed and total protein content was determined using BCA Protein Assay Kit (Pierce, Rockford, Ill). Local levels of IL-12, TNF-α, IL-10, IL-6, IL-1 ß, and IL-8 were measured and results stated as proportion of total protein.

Flow cytometry. To analyze circulating progenitor cells 2.5 mL of heparinized full blood samples were stained according to a modified protocol of the European Working Group on Clinical Cell Analysis.[1] Vital CD133+CD34+ CD45-7AAD- progenitor cells were determined by staining with fluorescein isothiocyanate (FITC)-conjugated anti-CD34, PE-conjugated anti-CD133, APC-conjugated anti-CD45, and 7AAD (BD Biosciences), additional measurements were performed to determine the absolute numbers using True Count beads (Becton Dickinson, Mountain View, Calif). CD34+CD31+ vascular endothelial growth factor (VEGF)-receptor-2+ endothelial progenitor cells were determined by staining with PE-conjugated anti-VEGFR2, FITC-conjugated anti-CD31 (Beckman Coulter, Fullerton, Calif) and APC-conjugated anti-CD34 (BD Biosciences). To analyze activated granulocytes surface expression of CD11b on CD45+CD15+ cells was determined using FITC-conjugated anti-CD11b, APC-conjugated anti-CD45, and PerCP-conjugated anti-CD15 (BD Biosciences). Fluorescence isotype-matched antibodies were used as controls. Flow cytometric analysis was performed using a FACS Calibur (Becton Dickinson). Fluorescence intensity of at least 200,000 cells was recorded and analyzed using CellQuest software (BD Biosciences, San Jose, Calif).

Culture assay of EPCs. Mononuclear cells were isolated from 5 mL EDTA-anticoagulated blood samples using Ficoll (Pharmacia Biotech, Freiburg, Germany) gradient separation. Mononuclear cells (5 × 10'6 cells per 24-well plate) were cultured on fibronectin coated cover slides in EGM-2 medium (Cambrex Clonetics, Baltimore, Md). After 4 days of culture, adherent EPCs were identified by expression of 1,10-dioctadecyl-3,3,30,30-tetramethylindocarbocyanine-perchlorate-labelled acetylated LDL (DiI-acLDL) incorporation and Ulex europaeus agglutinin-I (Sigma-Aldrich, Munich, Germany) binding by direct fluorescent staining. Four randomly selected fields from two cover slides were counted for DiI-ac-LDL and FITC-lectin-positive cells as a measure for EPCs.

Statistical analysis. Differences between more than 2 matched samples were tested by Friedman's test followed by Wilcoxon's matched-pairs signed-ranks test, and differences between the study group and the control group by the Mann-Whitney-Wilcoxon rank-sum test. A P value < .05 in the two-tailed test was regarded as significant.

RESULTS

Patients and procedural characteristics. In the present study, 45 patients with peripheral occlusive disease were included. Thirty-four patients underwent elective endarterectomy of the carotid artery, 11 patients of the femoral or iliac artery. Patients were either symptomatic with Fontaine classification stage II b or with transient ischemic attack. There was no statistical difference concerning age, risk factors, and medical treatment between carotid and femoral populations (Table I). All procedures were performed successfully. Patients with chronic inflammatory diseases or acute cardiovascular and cerebrovascular events, such as myocardial infarction, percutaneous coronary intervention, embolism and stroke, as well as surgery within the last 3 months were excluded. In the control group, all minor surgery procedures were performed successfully. No complication such as major bleeding, death, or cerebral events occurred.

Circulating CD34+CD133+, VEGFR2+CD34+ and endothelial progenitor cells. Hematopoietic and endothelial progenitor cells were measured before and after endarterectomy. Levels of circulating CD34+CD133+ cells were significantly lower after endarterectomy compared to preprocedural levels (Fig 1, *A*). Likewise postprocedural levels of VEGFR2+CD34+ cells and endothelial progenitor cells defined as DiI-ac-LDL and FITC-lectin double positive were decreased (Fig 1, *B and C*). This decrease in circulating progenitor cells was similar in femoral and carotid endarterectomy patients. In contrast, after minor surgery a 2.3 ± 0.9 fold increase in circulating CD34+ CD133+ cells was observed ($P = .05$).

Systemic inflammation after endarterectomy. Analysis of markers of systemic inflammation before and after endarterectomy showed a significant postprocedural increase in IL-6 and CRP, as well as an elevated surface expression of CD11b on circulating neutrophils (Fig 2, *A, B,* and *C*). Systemic levels of IL-12 and IL-1ß by contrast showed a significant decrease (Fig 2, *E* and *F*). Analyzing cytokines important for mobilization and homing of progenitor cells, we found that levels of G-CSF showed a signif-

Table I. Baseline characteristics

	Study patients (n = 45)	*Carotis endarterectomy (n = 34)*	*Femoral endarterectomy (n = 11)*	
Age, y	69 ± 1.5	69 ± 1.6	69 ± 3.7	*P* = .95
Sex, M/F (%)	34/11 (76/24)	25/9 (74/26)	9/2 (81/9)	*P* = .44
CAD, n (%)	13 (28)	10 (29)	3 (27)	*P* = .50
Hypertension, n (%)	29 (64)	21 (62)	8 (73)	*P* = .43
Diabetes, n (%)	13 (29)	9 (26)	4 (36)	*P* = .43
Hypercholesteremia, n (%)	22 (49)	16 (47)	6 (55)	*P* = .46
Nicotine, n (%)	9 (20)	7 (21)	2 (18)	*P* = .49
Beta-Blocker, n (%)	19 (42)	17 (50)	2 (18)	*P* = .14
ACE-Inhibitors, n (%)	19 (42)	17 (50)	2 (18)	*P* = .14
Nitrates, n (%)	8 (18)	4 (12)	4 (36)	*P* = .17
Statins, n (%)	26 (58)	20 (59)	6 (54)	*P* = .49
Calcium Antagonists, n (%)	3 (7)	3 (9)	0 (0)	*P* = .31
ASA/Clopidogrel, n (%)	40 (88)	30 (88)	10 (90)	*P* = .48

CAD, Coronary artery disease; *n*, number; *ACE*, angiotensin-converting enzyme; *ASA*, aspirin.

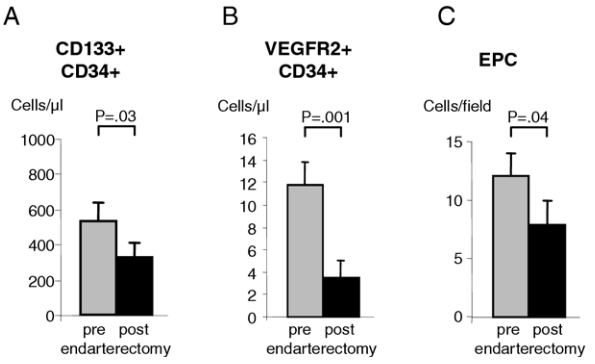

Fig 1. Circulating hematopoietic CD34+CD133+ (**A**). VEGFR-2+CD34+ (**B**) and endothelial progenitor cells (**C**) decrease after endarterectomy.

icant increase after endarterectomy (Fig 2, *F*). There were no differences between preoperative and postoperative cytokine levels between femoral and carotid populations. After minor surgery, we found a significant increase in IL-6 (2.01 ± 0.65 pg/mL; 12.93 ± 6.21 pg/mL; *P* = .01), IL-8 (7.61 ± 1.74 pg/mL; 9.02 ± 1.52 pg/mL; *P* = .02) and IL-10 (1.38 ± 0.08 pg/mL; 1.61 ± 0.07 pg/mL; *P* = .04). Pre- and postoperative IL-10 levels were higher in the control group compared to study population (0.67 ± 1.55 pg/mL; *P* = .01; 0.25 ± 1.09 pg/mL; *P* = .01). No differences or changes were seen in other measured cytokines.

Atherosclerotic plaque inflammation. From the attained atherosclerotic plaque material local levels of IL-12, TNF-α, IL-10, IL-6, IL-1ß, IL-8, and SDF-l were measured. Highest local concentrations were found for IL-8, IL6, and IL-1ß, and lowest levels were measured for IL12, IL10, and TNF-α (Table II). Since IL-6 production of vascular smooth muscle cells is known to contribute to atherosclerosis in ApoE deficient mice, we sought to categorize the inflammatory potential within the plaque according to IL-6 expression. Moreover, as infiltrating leukocytes may further aggravate local inflammation, we also assessed IL-8 levels. Because of the low number of patients, we showed the data categorized as IL-6 positive and negative plaques.

Forty-eight percent of all plaques were expressing IL-6. These were highly associated with local IL-8 levels (Fig 3, *A*), suggesting that IL-6 and IL-8 may reflect local pro-inflammatory changes within the plaque.

Association of local plaque inflammation and circulating progenitor cells. Analyzing the association of CD34+CD133+ circulating progenitor cells before surgery and specific patterns of inflammatory cytokines within local plaque tissue, we found that expression of IL-6 in plaque material was negatively associated with circulating levels of CD34+CD133+ progenitor cells (Fig 3, *B*) but not with circulating EPC or VEGFR2+CD34+ cells (data not shown). This association was only found for CD34+CD133+ cells preoperatively and was abolished after plaque removal. No association of circulating CD34+CD133+ cells with systemic cytokines was found.

DISCUSSION

Major findings of our study are as follows: (1) Vascular injury induced by endarterectomy results in a decline of both circulating hematopoietic and endothelial progenitor cells and (2) results in a systemic inflammatory response with a specific pattern of inflammatory cytokines. (3) Atherosclerotic plaques with detectable IL-6 were associated with lower numbers of circulating CD133+CD34+ progenitor cells. These results suggest that the local cytokine expression of atherosclerotic plaques may relate to the number of circulating progenitor cells. Considering circulating progenitor cells as potential repair mechanism, our results suggest that local IL-6-associated inflammation in atherosclerotic plaques may, by so-far undefined mechanisms, contribute to the recruitment of circulating CD133+CD34+ progenitor cells.

Circulating progenitor cells after endarterectomy. Tissue damage such as myocardial infarction,[1] severe burns, or bypass surgery[2] have been shown to increase the number of circulating progenitor cells. Circulating endothelial pro-

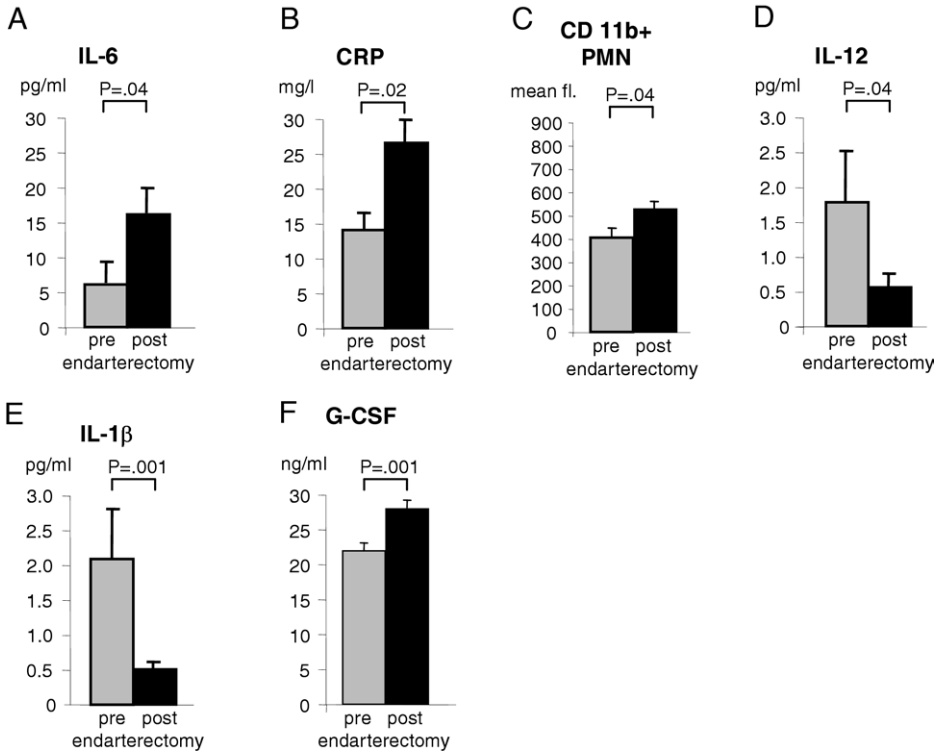

Fig 2. Systemic levels of interleukin (IL)-6 (**A**), C-reactive protein (**B**), surface expression of CD11b on circulating polymorphonuclear leukocytes (**C**), IL-12 (**D**), IL-1ß (**E**) and granulocyte colony-stimulating factor (G-CSF) (**F**) before and after endarterectomy.

Table II. Cytokine levels in plaque material

IL-12 (pg/mg)	4.1 ± 0.5
TNF-α (pg/mg)	2.9 ± 0.36
IL-10 (pg/mg)	1.9 ± 0.39
IL-6 (pg/mg)	6.7 ± 1.91
IL-1ß (pg/mg)	11.3 ± 1.97
IL-8 (pg/mg)	47.3 ± 19.67
SDF-l (pg/mg)	907.9 ± 116.42

Shown are mean values and standard errors.
IL, Interleuken; *TNF,* tumor necrosis factor; *SDF,* stromal derived factor.

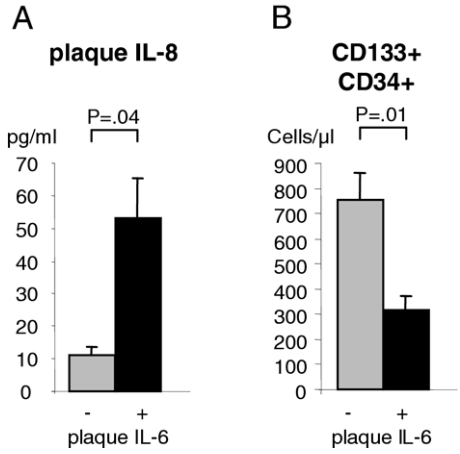

Fig 3. Relationship of interleukin (IL)-6 and IL-8 expression in atherosclerotic plaques (**A**) and negative association of local IL-6 expression and circulating CD34+CD133+ cells before endarterectomy (**B**).

genitor cells have been identified as an independent predictor for atherosclerotic disease progression,[9] so that cytokines that are involved in mobilizing and homeostasis of progenitor cells are of high clinical relevance. Increased progenitor cell release from the bone marrow is part of the host defence during inflammation and a result of injury-mediated release of stress signals. This release is induced by a wide range of mediators: cytokines such as G-CSF, GM-CSF, VEGF, SCF and chemokines such as IL-8, Mip-1α, Gro-ß, and SDF-1.[3] Recently, circulating IL-8 was identified as an independent predictor of progenitor cell mobilization in patients with acute myocardial infarction.[1]

Our study showed that after endarterectomy levels of circulating CD34+CD133+ cells, VEGFR2+CD34+ cells and endothelial progenitor cells were significantly lower compared to preprocedural levels. This decline of circulating progenitor cells seems at first sight to be contradictory to the above-mentioned study which showed rising progenitor cells after severe burns or bypass surgery.[2] One interpretation of the decrementing circulating progenitor

cells after endarterectomy could be a decreased mobilization. Experimental studies have identified posttraumatic bone marrow suppression. Looking at cytokines important for mobilization released by the postprocedural systemic inflammatory reaction, we found a significant rise in G-CSF levels, a cytokine well known to potently induce progenitor cell mobilization from bone marrow to peripheral blood. In our control group, in which patients underwent surgery without extensive vessel injury, we did not find a decrease in circulating progenitor cells; instead we found a trend for higher levels of circulating progenitor cells. In this context, we assume that circulating progenitor cells may decline after endarterectomy in spite of an increased mobilization, because of consumption due to recruitment to the site of vascular injury.

Systemic inflammatory changes after endarterectomy. The current understanding of atherosclerosis is characterized as a process of endothelial dysfunction, subendothelial inflammation and regenerative response. Increased vascular risk was demonstrated in epidemiological studies for patients with elevated levels of cytokines such as interleukin-6 and TNF-α, cell adhesion molecules such as intercellular adhesion molecule-1 and P-selectin, and acute-phase proteins such as C-reactive protein, fibrinogen and serum amyloid A.[7,8] So far, earlier investigations focused on histopathologic examinations of retrieved atherosclerotic plaque after endarterectomy[10] and some studies investigated plaque cytokine levels,[11,12] whereas little is known about systemic inflammatory changes after endarterectomy. We found that vascular injury by endarterectomy induced systemic inflammation with an increase in circulating CRP, IL-6, and neutrophil surface expression of CD11b, whereas other cytokines such as IL1ß and IL-12 decreased. Whereas, TNF-αIL-8 and IL-10 known to contribute to proinflamatory responses in sepsis[13] and acute coronary syndromes[1,14] remained unchanged. Cytokine changes after endarterectomy were different compared to changes after surgery without extensive vascular injury of the control group. Specific tissue damage of vascular injury may, thus, stimulate unique patterns of cytokine release that provoke distinct repair mechanisms.

Atherosclerotic plaque inflammation. Earlier studies with histopathologic examinations of atherosclerotic plaque after endarterectomy showed that unstable plaques were associated with extensive macrophage infiltration as a sign of local inflammation.[15] Elevated TNF-α, IL-8, and IL-6 levels have been found in atherosclerotic plaques compared to normal vessels.[16,17] Our study confirmed expression of IL-6, IL-8, and IL-1ß in human atherosclerotic plaques. The shown frequent and significant coexistence of IL-6 and IL-8 further underlines the importance of these cytokines in atherosclerotic plaque inflammation.

Association of local plaque inflammation and circulating progenitor cells. Whereas previous studies identified the number of progenitor cells as a predictor for atherosclerotic disease progression[8] or investigated the role of cytokines in atherosclerotic plaques,[7] this study shows, we believe for the first time, an association between local plaque inflammation and circulating progenitor cells. We found that high detectable levels of local IL-6 inflammation in atherosclerotic plaques were correlated with low preprocedural levels of circulating CD34+CD133+ progenitor cells that was abolished postoperatively. No such an association was seen for systemic levels of IL-6 or other cytokines. Recent studies suggest that atherosclerosis-prone areas have a very high endothelial turnover rate, which is regenerated, at least in part, by bone marrow–derived stem cells.[9,11] So far the underlying mechanisms of progenitor cell recruitment to the plaque is not completely understood but local cytokines like SDF-1 as well as local cell activation may contribute to this process.[3] Yet the number of circulating progenitor cells is not only altered by recruitment to the vessel wall but also by release from the bone marrow compartment. This process is driven by circulating cytokines eg, G-CSF in addition to local changes within the bone marrow.[3] Thus the association of vessel wall mediators with circulating number of progenitor cells may somehow relate to an altered recruitment of progenitor cells to the vessel wall whereas an association with circulating cytokines may relate to mobilization from the bone marrow.

Considering circulating progenitor cells as potential repair mechanism, local inflammation may contribute to vascular repair after endarterectomy. Therefore, a systemic decrease in circulating progenitor cells may result.

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AUTHOR CONTRIBUTIONS

Conception and design: AS, HM, RB, IO
Analysis and interpretation: AS, IO
Data collection: HM, BS, GB
Writing the article: AS, IO
Critical revision of the article: HM, BS, GB, RB
Final approval of the article: AS, HM, BS, GB, RB, IO
Statistical analysis: AS, IO
Obtained funding: IO
Overall responsibility: IO

REFERENCES

1. Schomig K, Busch G, Steppich B, Sepp D, Kaufmann J, Stein A, et al. Interleukin-8 is associated with circulating CD133+ progenitor cells in acute myocardial infarction. Eur Heart J 2006;27:1032-7.
2. Gill M, Dias S, Hattori K, Rivera ML, Hicklin D, Witte L, et al. Vascular trauma induces rapid but transient mobilization of VEGFR2(+)AC133(+) endothelial precursor cells. Circ Res 2001; 88:167-74.
3. Lapidot T, Petit I. Current understanding of stem cell mobilization: the roles of chemokines, proteolytic enzymes, adhesion molecules, cytokines, and stromal cells. Exp Hematol 2002;30:973-81.
4. Kocher AA, Schuster MD, Szabolcs MJ, Takuma S, Burkhoff D, Wang J, et al. Neovascularization of ischemic myocardium by human bone-marrow-derived angioblasts prevents cardiomyocyte apoptosis, reduces remodeling and improves cardiac function. Nat Med 2001;7:430-6.
5. Hansson GK, Libby P. The immune response in atherosclerosis: a double-edged sword. Nat Rev Immunol 2006;6:508-19.
6. Glass CK, Witztum JL. Atherosclerosis: the road ahead. Cell 2001;104: 503-16.

7. Mahmoudi M, Curzen N, Gallagher PJ. Atherogenesis: the role of inflammation and infection. Histopathology 2007;50:535-46.
8. Urbich C, Dimmeler S. Risk factors for coronary artery disease, circulating endothelial progenitor cells, and the role of HMG-CoA reductase inhibitors. Kidney Int 2005;67:1672-6.
9. Schmidt-Lucke C, Rossig L, Fichtlscherer S, Vasa M, Britten M, Kamper U, et al. Reduced number of circulating endothelial progenitor cells predicts future cardiovascular events: proof of concept for the clinical importance of endogenous vascular repair. Circulation 2005;111:2981-7.
10. Redgrave JN, Lovett JK, Gallagher PJ, Rothwell PM. Histological assessment of 526 symptomatic carotid plaques in relation to the nature and timing of ischemic symptoms: the Oxford plaque study. Circulation 2006;113:2320-8.
11. Frostegard J, Ulfgren AK, Nyberg P, Hedin U, Swedenborg J, Andersson U, et al. Cytokine expression in advanced human atherosclerotic plaques: dominance of pro-inflammatory (Th1) and macrophage-stimulating cytokines. Atherosclerosis 1999;145:33-43.
12. Braunersreuther V, Mach F, Steffens S. The specific role of chemokines in atherosclerosis. Thromb Haemost 2007;97:714-21.
13. Blackwell TS, Christman JW. Sepsis and cytokines: current status. Br J Anaesth 1996;77:110-7.
14. Steppich BA, Moog P, Matissek C, Wisniowski N, Kuhle J, Joghetaei N, et al. Cytokine profiles and T cell function in acute coronary syndromes. Atherosclerosis 2007;190:443-51.
15. Abi-Younes S, Sauty A, Mach F, Sukhova GK, Libby P, Luster AD. The stromal cell-derived factor-1 chemokine is a potent platelet agonist highly expressed in atherosclerotic plaques. Circ Res 2000;86:131-8.
16. Rus HG, Vlaicu R, Niculescu F. Interleukin-6 and interleukin-8 protein and gene expression in human arterial atherosclerotic wall. Atherosclerosis 1996;127:263-71.
17. Rus HG, Niculescu F, Vlaicu R. Tumor necrosis factor-alpha in human arterial wall with atherosclerosis. Atherosclerosis 1991;89:247-54.

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RECOUP THE LOUPES

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